carnitine-acylcarnitine translocase deficiency

Carnitine-acylcarnitine translocase (CACT) deficiency is a condition that prevents the body from using certain fats for energy, particularly during periods without food (fasting). Signs and symptoms of this disorder usually begin soon after birth and may include breathing problems, seizures, and an irregular heartbeat (arrhythmia). Affected individuals typically have low blood sugar (hypoglycemia) and a low level of ketones, which are produced during the breakdown of fats and used for energy. Together these signs are called hypoketotic hypoglycemia. People with CACT deficiency also usually have excess ammonia in the blood (hyperammonemia), an enlarged liver (hepatomegaly), and a weakened heart muscle (cardiomyopathy).

Many infants with CACT deficiency do not survive the newborn period. Some affected individuals have a less severe form of the condition and do not develop signs and symptoms until early childhood. These individuals are at risk for liver failure, nervous system damage, coma, and sudden death.

Frequency

CACT deficiency is very rare; at least 30 cases have been reported.

Genetic Changes

Mutations in the *SLC25A20* gene cause CACT deficiency. This gene provides instructions for making a protein called carnitine-acylcarnitine translocase (CACT). This protein is essential for fatty acid oxidation, a multistep process that breaks down (metabolizes) fats and converts them into energy. Fatty acid oxidation takes place within mitochondria, which are the energy-producing centers in cells. A group of fats called long-chain fatty acids must be attached to a substance known as carnitine to enter mitochondria. Once these fatty acids are joined with carnitine, the CACT protein transports them into mitochondria. Fatty acids are a major source of energy for the heart and muscles. During periods of fasting, fatty acids are also an important energy source for the liver and other tissues.

Although mutations in the *SLC25A20* gene change the structure of the CACT protein in different ways, they all lead to a shortage (deficiency) of the transporter. Without enough functional CACT protein, long-chain fatty acids cannot be transported into mitochondria. As a result, these fatty acids are not converted to energy. Reduced energy production can lead to some of the features of CACT deficiency, such as hypoketotic hypoglycemia. Fatty acids and long-chain acylcarnitines (fatty acids still attached to carnitine) may also build up in cells and damage the liver, heart, and muscles. This abnormal buildup causes the other signs and symptoms of the disorder.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- CACT deficiency
- carnitine-acylcarnitine carrier deficiency
- carnitine acylcarnitine translocase deficiency

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Elevated C16 and/or C18:1 acylcarnitine
  https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/C16_and-or_C18-1.pdf

Genetic Testing

- Genetic Testing Registry: Carnitine acylcarnitine translocase deficiency
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0342791/

Other Diagnosis and Management Resources

- Baby's First Test
  http://www.babysfirsttest.org/newborn-screening/conditions/carnitine-acylcarnitine-translocase-deficiency
- FOD (Fatty Oxidation Disorders) Family Support Group: Diagnostic Approach to Disorders of Fat Oxidation - Information for Clinicians
  http://www.fodsupport.org/clinicians.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html

- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Lipid Metabolism Disorders
  https://medlineplus.gov/lipidmetabolismdisorders.html
- Health Topic: Mitochondrial Diseases
  https://medlineplus.gov/mitochondrialdiseases.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- Carnitine-acylcarnitine translocase deficiency
  https://rarediseases.info.nih.gov/diseases/1123/carnitine-acylcarnitine-translocase-deficiency

Educational Resources

- Disease InfoSearch: Carnitine-Acylcarnitine Translocase Deficiency
  http://www.diseaseinfosearch.org/Carnitine-Acylcarnitine+Translocase+Deficiency/1115
- MalaCards: carnitine-acylcarnitine translocase deficiency
  http://www.malacards.org/card/carnitine_acylcarnitine_translocase_deficiency
- Orphanet: Carnitine-acylcarnitine translocase deficiency
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=159
- Screening, Technology, and Research in Genetics
  http://www.newbornscreening.info/Parents/fattyaciddisorders/CAT.html

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases (CLIMB)
  http://www.climb.org.uk
- FOD (Fatty Oxidation Disorders) Family Support Group
  http://www.fodsupport.org
- United Mitochondrial Disease Foundation
  http://www.umdf.org

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28carnitine-acylcarnitine+translocase+deficiency%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- CARNITINE-ACYLCARNITINE TRANSLOCASE DEFICIENCY
  http://omim.org/entry/212138

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